PHASE III COMMODORE TRIALS OF CROVALIMAB IN PAROXYMAL NOCTURNAL HEMOGLOBINURIA (PNH): IMPACT ON KIDNEY FUNCTION

Sasha Srecekovic,1 Cristian Brocchieri,2 Patty Leon,1 Nadiehs Balachandran,3 Marianne Uguen,2 Simon Bautois5

Summary

PHN is a rare, potentially life-threatening hematologic disease, arising from dysregulation of the complement pathway, for which C5 inhibition is the standard of care.1

In Phase II studies in patients with PNH, crovalimab demonstrated a favorable risk-benefit profile, indicating no impact on kidney function.

Methods

- In this analysis, data were pooled from the COMMODORE 1, COMMODORE 2, and COMMODORE 3 studies for safety and kidney function evaluation, including serum creatinine, as well as urine protein, albumin, and creatinine levels.
- Most patients had a baseline (BL) serum creatinine of ≤ 1.5 mg/dL (133 μmol/L).
- Grade 0 refers to patients with no abnormality, Grade 1 refers to patients with a baseline (BL) abnormality.
- Serum creatinine levels were comparable between patients receiving the loading dose (≥ 100 kg) and those receiving the weight-adjusted dose (≤ 100 kg).
- In the Phase III studies, serum creatinine was administered as a weight-based, tiered dosing schedule.

Results

- Overall, 111 patients received eculizumab and 377 patients received crovalimab as continued treatment or after switching from eculizumab or ravulizumab.
- Shifts in serum creatinine of ≥ 2 Grade from BL occurred in 4.5% (5/111) of patients receiving eculizumab and 6.5% (26/377) of patients receiving crovalimab.
- Among patients receiving crovalimab, shifts of ≥ 2 Grade from BL occurred in 24% (23/96) of patients treated with crovalimab as continued treatment or after switching from eculizumab or ravulizumab.
- In the Phase III studies, a T3H reaction (Grade 3 Henoch–Schoenlein purpura or Grade 3 arthralgia) occurred 8 days after switching treatment and had a duration of 9 days.
- The majority of T3H reactions, which are associated with formation of the eculizumab-c5a-crova complexes after switching treatment, were mild or moderate in severity.

Conclusions and Future Directions

- Serum creatinine shifts were comparable between patients receiving eculizumab and patients who switched from eculizumab or ravulizumab to crovalimab, or continued crovalimab treatment.
- Among patients who switched from eculizumab or ravulizumab to crovalimab, the occurrence of Grade 3 or 4 shifts was much lower than the median rate of potential onset of T3H symptoms, suggesting the creatinine shifts were not concerning as defined by being in the normal range.
- Overall, the Phase III data show the risk-benefit profile of crovalimab is favorable for the treatment of PHN.
- These data did not demonstrate any kidney concerns and are an encouraging indicator for the use of crovalimab in aHUS.

The novel C5 antibody crovalimab enables rapid and complete complement inhibition in patients with PNH, a threatening hematologic disease, arising from dysregulation of the complement pathway, for which C5 inhibition is the standard of care.1

Crovalimab is being evaluated as a treatment for aHUS in the Phase III COMMUTE and COMMUTE-p trials.

COMMUTE-p (NCT04559325): Pediatric patients

COMMUTE-e (NCT04661259): Adult/adolescent patients

COMMUTE-e and COMMUTE-p studies are evaluating crovalimab in patients with aHUS who are naïve to or switching from a C5 complement inhibition

References


Acknowledgments

The authors wish to acknowledge the clinical sites, patients, and families for their participation in the trials.

Disclosures

All SS and employees of Sanofi, Inc., CB, 160, 161, and SS are employees of F. Hoffmann-La Roche Ltd.

Contact

Sasha Srecekovic; srecekovs@gene.com

Presented at the 2023 American Society for Nephrology Kidney Week Meeting | Philadelphia, PA | November 1–5, 2023